REMARKS

The rejection of claims 3 and 6-7 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed.

Claim 7 of the present invention claims the step of preparing multilayered liposomes in accordance with claim 3, with the additional step of secondarily disrupting and mixing the multilayered liposomes by passing the multilayered liposomes through a high-pressure homogenizer. This is not inconsistent with the agitation step in claim 3, since it is a secondary operation which occurs after the multilayered liposomes are formed. The specification on page 24, line 26, through page 25, line 5 states that "the primarily prepared multilayered liposomes may pass, for example, through a high pressure homogenizer or a micro fluidizer under high pressure to obtain more uniformly multilayered liposomes".

Therefore, the present invention is directed to preparing multilayered liposomes using the method of claim 3 and then taking the primarily-produced multilayer liposomes formed without the use of a high-pressure homogenizer and further processing them in a secondary operation using a high-pressure homogenizer as indicated in claim 7. Accordingly, applicant does not understand the confusion alleged by the Examiner to exist between claims 3 and 7. If the Examiner still believes that claims 3 and 7 conflict, the Examiner is asked to please call applicants attorney at 212-589-4634, so that a further amendment to claim 7 can be made to overcome the rejection of claims 3 and 6-

7 under 35 USC 112, second paragraph. As indicated above, applicant does not believe claims 3 and 7 are confusing and does not consider claim 3 indefinite. Accordingly, applicant requests that the rejection under 35 USC 112, second paragraph, be withdrawn.

The rejection of claims 3 and 6-7 under 35 USC 103(a) as being unpatentable over Popp (US Pub. 2006/0029657) in combination with Foldvari (USP 5,853,755) and optionally in further combination with Needham (US Pub. 2002/0102298) is respectfully traversed.

Claim 3 is directed to a method and not to a composition in which multilayered lipsomes are formed by dissolving oil phase components comprising squalene, sterols, ceramide, neutral lipids or oils, fatty acids and lecithins, in an organic solvent, dissolving the aqueous phase components at 50°C to 75°C and then mixing the dissolved components by agitating the mixture at 500 – 9000 rpm without the use of a high-pressure homogenizer. This procedure forms multilayered lipsomes in a particle size range of 800 – 10,000 nm provided squalene is present in the range of 0.1-10 wt.%, the sterols are in the range of 0.1-5 wt.%, the ceramide is in a range of 0.1-10 wt.%, the neutral lipids or oils are in an amount from 0.1-20 wt.%, fatty acids is present in an amount of 0.1-20 wt.% and lecithins are present in the amount of from 0.1-5 wt.%, based on the total weight of the liposomes. The presence of <u>both</u> fatty acids and squalene are critical to the method of the subject invention for forming multilayered liposomes which will remain stable and uniform in size within a narrow size range of

800 – 1000 nm and will not grow in size over a time period of less than one year as is known to be conventional.

This was confirmed in accordance with examples 1, 2, 3 and 4 of the specification. Example 1 shows that the prepared multilayered liposomes having the wt.% composition recited in claim 3 will form in a narrow size range of 800-1000 nm and that the number of liposome layers formed will be in a range of between 3 - 20 as shown in Example 2. The number of liposome layers formed has been added as new claim 12.

Example 3 shows the result of measuring the stability of the liposomes which confirms the finding that after 12 months, the liposomes remain uniform and in the same narrow size range when formed, and are thermodynamically stable. As indicated in Table 3, conventional multilayer liposomes are not stable, are not uniform in size and grow in size by more than 50% over time (comparative examples 1, 2 and 4).

Example 4 of the subject invention confirms that the multilayer liposomes of the present invention as claimed have an excellent subcutaneous absorption rate (see Table 4).

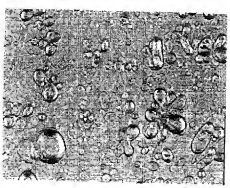
The Popp reference cited by the Examiner recites a composition excluding fatty acids and does not teach agitating the mixture without the use of a high-pressure homogenizer. Instead, the Examiner seems to believe that even though it does not teach fatty acids and is silent regarding the conventional use of a high-pressure

homogenizer, it must somehow be implicit that multilayered liposomes will be formed of uniform size in a range between 800 - 1000 nm. However, without the presence of fatty acids and without a teaching of not using a high-pressure homogenizer, there is no basis for this assumption, and certainly no basis for using the concentration of components as claimed to yield multilayered liposomes in a narrow size range of between 800 - 1000 nm. . This is neither expressly taught or implicit from the teaching of Popp.

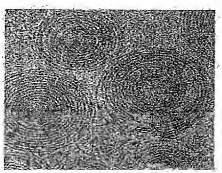
The Foldvari teaching does not teach adding squalene, which is critical to the subject invention. Instead, Foldvari relates to multilamellar vesicles, for topical delivery containing a phospholipid, a ceramide oil, cholesterol and fatty acids, to form multilayered liposomes in a wide size range of 1-30 micrometers in size. Please note that the liposomes in Foldvari have a high variety of sizes and shapes which appear to be both linked to or separated from one another. There is no teaching in Foldvari that the liposomes will be relatively uniform in size within a narrow range and be thermodynamically stable so as not to change in size or shape over time.

In contrast, those prepared according to the present invention have uniform shape, close to thermodynamically stable circles, and form concentric circles (FIG 4; see below).

[D2]



[Present Invention]



-It is clear that, as opposed to the oil-phase components having no squalane as is taught in Foldvari, the multilayer liposomes formed in accordance with the present invention using squalane are highly uniform in both shape and size of small size and are highly stable.

As supported by the specification of the present invention (Tables 2 and 3), liposomes can have different properties, sizes and shelf-lives according to a combination of constitutional elements and their composition ratio. To derive the thermodynamically stable multilayered liposomes of the present invention which are uniform in size and shape and maintain their size after 1 year the oil-phase components must include both fatty acids and squalene.

Claims 6 and 7 depend from claim 3 and are believed patentable for the same reasons as given above.

New claim 12 has been added as a dependent claims, dependent upon claim 3 to specify the number of liposome layers in a range of from 3-20 which is supported in Example 2.

Reconsideration and allowance of claims 3, 6, 7 and 12 is respectfully solicited.

Respectfully submitted,

Eugene Lieberstein
Reg. No. 24,645

Customer # 79681
BAKER & HOSTETLER LLP
45 Rockefeller Plaza
New York, NY 10111
Tel: 212-589-4634 / Fax: 212-589-4201

CERTIFICATE OF TRANSMISSION

I hereby certify that this Amendment is being submitted to the USPTO via EFS-Web addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450, on April 20, 2011.

By _____